Brief report: Mechanism of extravasation of infused stem cells.

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Public Summary:
order for bloodborne stem cells to be effective in tissue regeneration, cells must cross vessel walls and enter the parenchyma. Although such transmigration does occur, the mechanism remains elusive. Leukocytes invade tissue by diapedesis; stem cells are commonly assumed to do likewise, but evidence is lacking. Cardiac-derived regenerative cells and multicellular cardiospheres (CSPs) were infused into the coronary vessels of rat hearts. Serial histology revealed a novel mechanism of cell transmigration, "active vascular expulsion," which underlies the extravasation of infused cells and cell aggregates. In this mechanism, the vascular barrier undergoes extensive remodeling, while the cells themselves are relatively passive. The mechanism was confirmed in vivo by serial intravital microscopy of CSP extravasation in a dorsal skin flap model. Integrins and matrix metalloproteinases play critical roles in active vascular expulsion. In vitro models revealed that active vascular expulsion is generalizable to other stem cell types and to breast cancer cells. Recognition of active vascular expulsion as a mechanism for transvascular cell migration opens new opportunities to enhance the efficacy of vascularly delivered cell therapy.

Scientific Abstract:
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